Remarks

Claims 1-3, 7-8 and 42 are novel over Schwartz.

Schwartz et al. discloses exclusively immunostimulatory sequences in which the C residue of a CG dinucleotide is modified by addition to C-5 and/or C-6 of an electron withdrawing (hydrogen bond acceptor) group. In fact, Schwartz et al. specifically defines "modified ISS" in this manner. (See page 7, lines 13-15 and throughout). All of the oligonucleotides of claim 1 contain modified cytosine residues which have added electron donating groups (hydrogen bond donors). Claim 3 has been amended to remove the term "hydrogen bond donor" and therefore bring it into proper dependent form upon claim 1. With respect to aracytosine, this nucleoside does not contain an electron withdrawing group, and therefore cannot be a "modified C residue of a CG dinucleotide" according to Schwartz. Closer inspection of Schwartz (see page 11, lines 27-32) shows that while Schwartz lists arabinose as a possible sugar analog for a C nucleoside in the CG dinucleotide of the modified ISS, it certainly does not envisage it as a modified C in a CG dinucleotide for such purpose, which would be inconsistent with Schwartz's definition of modified ISS.

Accordingly, claims 1-3, 7-8 and 42 are novel over Schwartz. Applicants respectfully request that this rejection be withdrawn.

Claims 1-3, 7-8 and 40 are novel over Zuo et al.

Zuo et al. discloses a study of oxidative damage to 5-methylcytosine in a DNA copolymer of polydG-dmC through oxidation of the copolymer by gamma irradiation or hydrogen peroxide. Zuo et al. discloses that thymine glycol was virtually the only product formed as a result of oxidation of the 5-methylcytosine residues within the DNA alternating co-polymer (see Discussion, page 3242). Totally contrary to the assertion in the presently maintained rejection that Zuo et al. does not disclose "an oligonucleotide compound comprising a dinucleotide of formula 5'-pyrimidine-purine-3', wherein the pyrimidine is a non-natural pyrimidine nucleoside" (emphasis added) and that "the compound taught by Zuo et al. comprises ... 5'-hydroxycytosine". At best, Zuo et al. teaches an undefined and complex mixture of oligonucleotides, polynucleotides or mononucleotides which may or may not include a 5'-hydoxycytosine within a CG

dinucleotide. Zuo et al. certainly does not disclose how to obtain an oligonucleotide compound from such a complex mixture, even if a molecule of such species may (or may not) appear in the complex mixture. Zuo et al. clearly does not put the claimed oligonucleotide in possession of one skilled in the art with, as required by *In re Spada* and a litany of other Federal Circuit decisions. Accordingly, Applicants respectfully request that this rejection be withdrawn.

Amended claims 1 and 2 and claims 3, 7 and 41 are novel over Butkus et al.

Claims 1, 2 and 41 have been amended to change N4-alkylcytosine to N4-ethylcytosine. Accordingly, Applicants respectfully submit that this rejection has been overcome and should be withdrawn.

Amended claims 1-2, claim 7 and amended claim 39 are novel over Kreutzer et al.

Claims 1 and 2 have been amended to remove "5-hydroxycytosine". Claim 6 has been cancelled. Claim 39 has been written in independent form and amended to include a limitation to a phosphorothioate internucleoside linkage. Support for this latter amendment is found at page 10, line 27-page 11, line 1. While the rejection recites "5-hydroxymethylcytosine", review of the citer reference leads Applicants to believe that "5-hydroxycytosine" was intended. Applicants respectfully submit that these amendments overcome the present rejection and request that this rejection be withdrawn.

Claim 43 is nonobvious and patentable over Schwartz in view of Bennett et al.

Schwartz and Bennett et al. cannot properly be combined because Schwartz deals exclusively with ISS containing a CG dinucleotide wherein the C base has been modified to add an electron withdrawing group. Bennett et al. teaches substitution of thiouracil, which adds an electron donating group. Neither reference provides a reasonable expectation that a thiouracil residue in place of a C in a CG dinucleotide would provide an immunomodulatory effect. Accordingly, Applicants respectfully request that this rejection be withdrawn.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned.

Respectfully submitted,

By _____
Wayne A. Keown, Ph.D.
Registration No. 33,923
Direct Dial: 781/933-6630

11/18/05

KEOWN & ASSOCIATES
500 WEST CUMMINGS PARK
SUITE 1200
WOBURN, MA 01801
Telephone: 781/938-1805
Facsimile: 781/938-4777